# Peptide-lipid membrane interaction: influence of free fatty acids-deriving alterations in host membrane's thermodynamic stability

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The binding of peptides/proteins to membrane surfaces is crucial in several biological events and is often accomplished through lipid-interacting protein domains. Generally, many peptides have been shown to approach the cell membrane by means of nonspecific interactions [1], which drive, if possible, the subsequent insertion of the peptide's hydrophobic portions within the phospholipid bilayer. However, peptides/proteins functionalities and interaction with membrane also depend on the physicochemical properties of the lipid bilayer itself [2,3]. Therefore, the presence and the effects deriving from external perturbing agents within the cell lipid bilayers might significantly affect the resulting peptide-membrane binding.

In this frame, this work was focused on the effects that the presence of Free Fatty Acids (FFAs), which are naturally present in biological membranes, may have on peptide-membrane interaction [4]. For this purpose, nisin, a small cationic peptide known for its ability of interacting with cell membranes both directly and by a receptor-mediated way [5], was selected as a model for the peptide-membrane interaction study. Furthermore, basing on the thermodynamic information achieved through the previous studies [6,7], a model cell membrane was designed and prepared as reference liposome system by combining specific percentages of DMPC, DPPS and DOPC in order to consider the main compositional aspects (phospholipid headgroup, tails, presence of unsaturations) and to resemble the thermal stability profile commonly observed in both real cell membranes and highly-representative artificial ones in terms of cooperativity and enthalpy contributions to the gel-to-liquid crystalline phase transition. Nisin-vesicle interaction was investigated through micro-DSC and fluorescence spectroscopy in FFAs-free and FFAs-containing liposomes at physiological pH (pH 7.4). The effects of six different FFAs on membrane stability were evaluated, namely two saturated FFAs (palmitic acid and stearic acid), two monounsaturated FFAs (the *cis*-unsaturated oleic acid and the *trans*-unsaturated elaidic acid) and two *cis*-polyunsaturated FFAs (the ω-6 linoleic acid and the ω-3 docosahexaenoic acid or DHA).

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